On Drug Pedigree and RFID in the Pharmaceutical Supply Chains: A Recommendation to the FDA *Executive Summary*

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Protecting the Public Health

THE U.S. Food and Drug Administration (FDA), one of the nation's oldest and most respected consumer protection agencies, is charged with promoting and protecting the public health by helping safe and effective products reach the market in a timely fashion, by monitoring products for continued safety post marketization, and by providing the public with accurate science-based information needed to improve health. The increasing instances of counterfeit drug products entering the marketplace coinciding with a renewed federal emphasis on public safety and security has accelerated the FDA's effort to eliminate this potentially deadly criminal activity. And, the FDA is turning to new technologies in their continuing fight to increase public safety and eliminate the presence of counterfeit drugs in the legal distribution channels.

The Prescription Drug Marketing Act (PDMA), in 21 USC 353(e)(1)(A), has a Statement of Origin, or 'Pedigree,' requirement. The implementation of the Pedigree requirement and the FDA rules for its implementation, primarily 21 CFR 203.3(u) and 21 CFR 203.50, have been stayed until December 2006. The FDA is presently considering whether to further the stay or let the provisions at issue go into effect in December 2006.

The FDA should allow the PDMA Pedigree provisions to go into effect in December 2006. The implementation of these provisions is technically feasible, and has been for several years. The failure of the industry to act to implement the PDMA Pedigree provisions since their finalization in 2000 should not be taken as an indication of the technical or economic infeasibility of providing pedigrees. New technologies, such as Radio Frequency Identification (RFID) technologies, that can enhance the Pedigree functionality or can do it better or with less cost or more benefit are continually becoming available on the market. The PDMA Pedigree provisions need not wait for a perfect technical solution to exist prior to them going into effect, particularly since it is not clear that this perfect solution exists. Furthermore, the active enforcement of the PDMA Pedigree provisions will hasten the development of new, better, and less expensive solutions.

In the remainder of this brief note, I provide my conclusions and best guess opinions as to the feasibility and implementation timings for the technologies and policies required to implement the PDMA Pedigree provisions and related functional capabilities. The primary technical components required to implement or that can be used to enhance the implementation of Pedigree are broadly categorized as: Serialization, Automated Identification Technologies, and Pedigree.

Serialization, Automated Identification, and Pedigree are distinct concepts that have technologically different requirements. As such, they should be separated in the regulations and in their suggested or required implementation timelines.

I summarize my primary conclusions for each of these categories in the remainder of this note.

Serialization Schemes for Unique Item Identification

The pharmaceutical industry does not have but requires a commonly used unique identification scheme that may itself only be a common representation for multiple distinct unique identification schemes. ***The pharmaceutical industry, under the guidance of the FDA, must agree to a unique identification scheme in a very short period of time.*** And, I suggest **July 1, 2006** as a deadline for agreement of this scheme.

The goal of serialization is to allocate a unique and persistent identifier to each item. This identifier can be used in a similar fashion to the Social Security Number as the basis of establishing the authenticity of an item, and the information associated with that item, throughout its lifespan.

Within the drug distribution chains, each item should be assigned a unique identifier at the point of manufacture, and in the case of repackers, at the point of packaging. Each end item, such as each vial, bottle, and blister pack, (and potentially even each tablet), each case, each tote, and each pallet, should be assigned distinct unique identifiers. The primary requirements for a unique identification scheme are stated below.

The unique identifiers used at all levels should be persistent, one-time use numbers. The reuse of identifiers prevents the identifier from being used as the sole piece of information in determining an items true identity.

The unique identification scheme(s) and their representations used should have sufficient capacity to uniquely identify every item for at least the next century. The length of time

here is arbitrary. The point is that duplication of numbers either due to encoding restrictions or identification scheme restrictions should be extremely long in duration, and ideally, is never forced to occur.

The unique identification scheme and all of its possible encodings should allow the unambiguous encoding of unique identifiers from multiple namespaces. The U.S. Department of Defense UID Policy provides an excellent example of how to encode identifiers from multiple identifiers within a single namespace. While we are discussing the U.S. specifically, the drug manufacture and distribution industry is global with many unique identification schemes either required or in common use around the world. Provisions to incorporate these schemes should be made.

The unique identification scheme should allow for privacy and security. The serialized structure used by the companies must minimize the security and privacy exposure created by the use of a unique item identifier. If the only carrier of the unique identifiers is a bar code, minimal security and privacy exposure is created by allowing the identifier to encode product information such as manufacturer, product type, dosage level, and packaging. An NDC or serialized NDC is possible. However, when RFID technology is used, the non-line of sight capabilities of the RFID tag allow anyone to read the least expensive, promiscuous tags. It is reasonable to expect that most companies will use these least expensive promiscuous tags; therefore, the identifier stored on the promiscuous portion of the RFID tag cannot reveal significant information about the potentially unseen product. In the ideal world, the unique identifier stored on the RFID tag is a purely random identifier. We do not live in an ideal world, and this purely random identifier is impractical. A practical solution will be for the unique identifier to encode the manufacturer's identifier and a random serial number. Revealing the product's manufacturer does not reveal significant information.

The unique identification scheme should not force users to encode the NDC number or a serialized version thereof. NDCs are non-unique, encode information about the item and are already encoded in a linear bar code per 21 CFR 201.25.

AUTOMATED IDENTIFICATION SYSTEMS

Automated identification systems, such as linear bar codes, 2D bar codes, and RFID systems, are used to automate the collection of data and information during the course of normal business operations. Multiple automated identification systems exist, and ***multiple automated identification technologies should be used to encode possibly different information within or on a drug item.*** It is incumbent upon the regulators to specify which technologies will be used and what information will be encoded within each automated identification technology.

Linear bar codes encoding an NDC or HIBC code are required per 21 CFR 201.25. Linear bar codes do not efficiently encode serialized identifiers. Therefore, ***in addition to the marking required by 21 CFR 201.25, I recommend that a 2D bar code that encodes the items serialized identifier be required on items.*** The timings for these new markings can be phased in, beginning with highly counterfeited products in ***December 2006.*** Provisions should be made to allow for additional information beyond the serialized identifier to be stored in the 2D bar code. This will enable additional security and authentication features to be added seamlessly. For example, a random encoded within the same 2D structure as the item's serialized identifier provides a significantly higher level of security and counterfeit detection capability than does simply encoding the serialized identifier.

RFID systems are the third widely available and proven automated identification technology commercially available today. RFID holds the promise of greatly improving supply chain efficiencies, improving visibility and ultimately improving the safety and security of the products being monitored with a lower overall total cost of ownership. RFID holds this promise, but it has not yet delivered on this promise in any industry.

For this reason, ***I recommend that the FDA continue suggesting, but not mandating, the use of RFID technologies where an RFID tag encodes at least a serialized identifier. A suggested phased deployment beginning with cases and pallets in the near term, beginning January 2007, and suggesting that all items be RFID enabled by January 2010.***

The use of RFID tags will require that a back-up technology be used to encode a serialized identifier for the item. Note that the identifier encoded by the back up technology need not be the same identifier stored in the RFID tag. I recommend 2D bar codes as the back up technology.

The use of RFID systems will also require verification that the exposure to radio frequency radiation does not cause a decrease in the efficacy of products. The Healthcare Research Initiative at MIT is presently developing a methodology and performing experiments to determine if there is any non-thermal impact from RF radiation. The first phase of these experiments will be completed by the end of March 2006 and will be shared with the FDA at that time.

The cheapest, and therefore, most widely deployed RFID tags will be promiscuous and store mainly the item's serialized identifier. Promiscuous RFID tags may be used to great benefit, and high security tags are not warranted in most applications and scenarios involving drugs. Those persons that are concerned about privacy and being tracked by the unique identifiers stored on RFID tags may destroy the tags or place RFID tagged objects in a foil lined bag (preferably provided free of charge and as part of standard operating procedure by the pharmacist) to prevent unwanted reads.

Drug Pedigree

A drug pedigree is simply a mechanism to provide information that may be authenticated to help prove the authenticity of a product. Pedigrees may be based on paper or may be electronic. They may utilized product identifiers or unique item identifiers. And, they may utilize, or not, any of the available automated identification technologies, which is to say that pedigrees are independent of the automated identification technology used to obtain the identifier information.

The strongest pedigrees utilize unique identifiers at the item level. Unique identifiers at the case level will work provided

that their is a way to verify the integrity of the case. In this way, ***pedigrees can be maintained on physically encapsulated products;*** thereby, reducing the burden in generating appropriate pedigree documentation. Once a case is opened, its contents cannot be automatically authenticated unless it too has a pedigree.

Pedigrees must begin at the manufacturer. 21 USC 353(e)(2)(A) exempts manufacturers and authorized distributors of record (ADRs) from providing drug pedigrees. If an ADR purchases products only from the manufacturer and maintains product inventory that came directly from the manufacturer, then the ADR is acting as an agent of the manufacturer and can be trusted to not have any counterfeit products. However, there is no prohibition against an ADR purchasing products or maintaining inventories of products that did not come directly from the manufacturer. By not providing pedigrees on these products, the ADRs will be laundering the products and provide a mechanism for counterfeit products to become 'clean.'

The FDA recognized this potential in 21 CFR 203.50 where the pedigree is required to begin at the first sale by the manufacturer. It is nearly impossible to distinguish between two products with different life histories if those products are not uniquely identified with distinct unique identifiers. Therefore, serialization is essential to providing accurate pedigrees within the complex supply chain that exists for drug distribution.